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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/024,599	12/21/2001	Daniel M. Cimbora	2318-278-II	2443

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ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
SANG, HONG	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 09/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/024,599	CIMBORA ET AL.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2001*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-171* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-171* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

100

DETAILED ACTION

RE: Cimbora et al.

Election/Restrictions

I. Claims I-4 and 147-165, drawn to an isolated protein complex comprising two proteins, an isolated polypeptide, classified in class 530, subclass 300.

II. Claims 5-6 and 166-167, drawn to an isolated antibody selectively immunoreactive with a protein complex of claim I, an isolated antibody which is specifically immunoreactive with the isolated polypeptide, classified in class 530, subclass 387.1.

III. Claims 7-26, drawn to a method for diagnosing a physiological disorder in an animal comprising assaying for (a) whether a protein complex of claims 1 is present in a tissue extract; (b) the ability of proteins to form a protein complex of claims 1; (c) a mutation in a gene encoding a protein of a protein complex of Claim 1, classified in class 424, subclass 9.1.

IV. Claims 27-29, drawn to a non-human animal model for a physiological disorder, wherein the genome of said animal or ancestor thereof has been modified such that the formation of a protein complex of Claim 1 has bee altered, wherein the biological activity of a protein complex of Claim 1 has been altered by an antibody, by a small molecule, classified in class 800, subclass 8.

V. Claims 30 and 38-39, drawn to a cell, a cell line in which the genome of cells of said cell line has been modified to produce at least one protein complex of Claim

1, or to eliminate at least one protein of a protein complex of Claim 1, classified in class 435, subclass 325.

VI. Claims 40-45 and 117-145, drawn to a composition comprising the first expression vector having a nucleic acid encoding a first protein or a homologue or derivative or fragment thereof, and a second expression vector having a nucleic acid encoding a second protein or a homologue or derivative or fragment thereof; a host cell comprising said first and second expression vector, XVI; an isolated nucleic acid, a host cell comprising the isolated nucleic acid, classified in class 435, subclass 320.1.

VII. Claims 46-50, drawn to a method for screening for drug candidates capable of modulating the interaction of proteins of a protein complex 1, comprising the step of measuring the amount of protein complex formed in the presence or absence of said drug, classified in class 435, subclass 7.1, for example.

VIII. Claims 51-52, 54-55, 57-58, 66-67, 69-70, 73-74, 76-77, 79-80, 82-83 and 87-88 drawn to a drug, a modulator, an inhibitor useful for treating a physiological disorder, classified in class 514, subclass 2, for example.

IX. Claim 53, drawn to a method for screening for drug candidates useful in treating a physiological disorder comprising the step of measuring the activity of the protein of the protein complex of Claim 1 in the presence or absence of said drug, classified in class 535, subclass 4.

X. Claims 56, 75 and 84-86, drawn to a method for selecting modulators of a protein complex of Claim 1 comprising the step of determining the presence or absence

of binding of said test compound to said protein complex, classified in class 435, subclass 7.1.

XI. Claims 59-66, 68 and 71-72 drawn to a method for selecting modulators of an interaction between a first protein and a second protein of the protein complex 1 comprising the step of determining the interaction between said first protein and said second protein, classified in class 435, subclass 7.1.

XII. Claims 78-79, 81 drawn to drawn to a method for selecting modulators of an interaction between a first protein and a second protein of the protein complex 1 comprising the step of providing atomic coordinates defining a 3D structure of a protein complex and designing or selecting compounds capable of modulating the interaction between a first polypeptide and a second of polypeptide, classified in class 435, subclass 4, for example.

XIII. Claims 89-116, drawn to a method for modulating, in a cell, a protein complex of Claim 1, comprising administering to said cell a compound capable of modulating said protein complex, a method for modulating neuronal death in a patient having a physiological disorder comprising modulating a protein complex of Claim 1; a method for treating a physiological disorder comprising administering to a patient a compound capable of modulating a protein complex of Claim 1; a method for modulating activity in a cell of a protein, said protein being first protein or a second protein of the protein complex of Claim 1classified in class 514, subclass 2.

If applicant elects this group for prosecution on the merits, applicant is additionally required to elect a single type of compound from Claims 90, 95, 100 and 105. This election should not be construed as an election of species and rather is a restriction. Each of the compounds listed in Claims 90, 95, 100, 105 and 124 is structurally distinct molecule which requires separate searches.

XIV. Claim146, drawn to a microarray comprising the isolated nucleic acid, classified in class 536, subclass 24.31, for example.

XV. Claim 168-170, drawn to a protein microarray comprising the isolated polypeptide, classified in class 436, subclass 518, for example.

XVI. Claims 171, drawn to a method for making an isolated polypeptide, classified in class 435, subclass 69.7, for example.

2. The inventions are distinct, each from the other because of the following reasons:

3. Groups I and II are patentably distinct for the following reasons:

While the inventions of both Group I and Group II are polypeptides, in this instance the polypeptide of Group I is a single chain molecule that functions as an enzyme, whereas the polypeptide of Group II encompasses antibodies including IgG which comprises 2 heavy and 2 light chains containing constant and variable regions, and including framework regions which act as a scaffold for the 6 complementarity determining regions (CDRs) that function to bind an epitope. Thus the polypeptide of Group I and the antibody of Group II are structurally distinct molecules; any relationship between a polypeptide of Group I and an antibody of Group II is dependent upon the

correlation between the scope of the polypeptides that the antibody binds and the scope of the antibodies that would be generated upon immunization with the polypeptide. Moreover, the polypeptide of Group I can be used in another materially different process as opposed to its use for production of the antibody of Group II, such as in a pharmaceutical composition, or in assays for the identification of agonists or antagonists of the protein.

Furthermore, searching the inventions of Group I and Group II would impose a serious search burden. The inventions have a separate status in the art as shown by their different classifications. A polypeptide and an antibody which binds to the polypeptide require different searches. An amino acid sequence search of the full-length protein is necessary for a determination of novelty and unobviousness of the protein. However, such a search is not required to identify the antibodies of Group II. Furthermore, antibodies which bind to an epitope of a polypeptide of Group I may be known even if a polypeptide of Group I is novel. In addition, the technical literature search for the polypeptide of Group I and the antibody of Group II are not coextensive, e.g., antibodies may be characterized in the technical literature prior to discovery of or sequence of their binding target.

4. Group I and Groups III, VII, IX-XII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the

protein complex or polypeptide can be used to generate antibodies as opposed to its use for diagnosing, drug screening and treating diseases.

Searching the inventions of Group I and Groups III, VII, IX-XII together would impose serious search burden. The inventions of Groups I and III, VII, IX-XII have a separate status in the art as shown by their different classifications. Moreover, in the instant case, the search for the protein complex, polypeptides and the methods of diagnosing, screening, modulating and treating diseases are not coextensive. Groups III, VII, IX-XII encompass molecules which are claimed in terms of gene mutation, measuring the amount of protein complex, measuring the activity of the protein, measuring the binding between drug and protein, screening for drugs, which are not required for the search of Group I. Moreover, the search for Groups III, VII, and IX-XII would require a text search for the methods. Prior art which teaches a protein complex or a polypeptide would not necessarily be applicable to the method of using the protein complex or a polypeptide. Moreover, even if the protein complex or the polypeptide product was known, the method of using the product may be novel and unobvious in view of the preamble or active steps.

5. Group I, IV, V, VIII, XV, XIV are patentably distinct products. Group I is a protein complex, a polypeptide. Group IV is transgenic animal, and Group V is a cell or a cell line, Group VIII is a drug which can modulate the activity of the protein complex. The drug can be a peptide, an antibody, a small molecule, a nucleic acid, an antisense nucleic acid, etc., Group XIV is a device, comprising many other nucleic acids which do not encode the protein complex or polypeptide of Group I, Group XVI is a device

comprising many structurally distinct antibodies which do not specifically bind to the protein complex or polynucleotide of Group I, therefore they are directed to products that are distinct both physically and functionally, are not required one for the other. Moreover, each is capable of separate manufacture and use, and each requires separate searches.

6. The polypeptide of Group I and expression vector of Group VI are patentably distinct inventions for the following reasons. Polypeptides, which are composed of amino acids, and polynucleotides of the expression vector of Group VII, which are composed of purine and pyrimidine units, are structurally distinct molecules; any relationship between a polynucleotide and polypeptide is dependent upon the information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. Because the protein product can be made by another and materially different process, such as by synthetic peptide synthesis or purification from the natural source, and the DNA can be used for processes other than the production of the protein, such as nucleic acid hybridization assay, the inventions of Groups I and VI are patentably distinct.

Furthermore, searching the inventions of Groups I and VI together would impose a serious search burden. In the instant case, the search of the protein complex or the polypeptides and the polynucleotides are not coextensive. The inventions of Groups I and VI have a separate status in the art as shown by their different classifications. In cases such as this one where descriptive sequence information is provided, the sequences are searched in appropriate databases. There is search burden also in the

non-patent literature. Prior to the concomitant isolation and expression of the sequence of interest there may be journal articles devoted solely to polypeptides which would not have described the polynucleotide. Similarly, there may have been "classical" genetics papers which had no knowledge of the polypeptide but spoke to the gene. Searching, therefore is not coextensive. In addition, the polypeptide claims include polypeptides having 75% identity to the sequence identified. This search requires an extensive analysis of the art retrieved in a sequence search and will require an in-depth analysis of technical literature. Furthermore, a search of the nucleic acid molecules of Group VI would require an oligonucleotide search, which is not likely to result in relevant art with respect to the polypeptide of Group I. As such, it would be burdensome to search the inventions of Groups I and VI together.

7. Groups I and XVI are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the protein complex or polypeptide of Group I can be made by peptide synthesis or can be isolated from natural source.

Searching the inventions of Groups I and XVI together would impose serious search burden. The inventions of Groups I and XVI have a separate status in the art as shown by their different classifications. Moreover, in the instant case, the search for the polypeptides and the method of making the polypeptide using expression vector are not coextensive. Group XVI encompasses molecules which are claimed in terms of

expression vector and host cell, which are not required for the search of Group I. Moreover, the search for Group XVI would require a text search for the method of making an isolated polypeptide.

8. Group II and Groups III, VII maybe related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody can be used to treat diseases as opposed to its use for detecting the protein complex.

Searching the inventions of Group II and Groups III, VII together would impose serious search burden. The inventions of Groups II and III, VII have a separate status in the art as shown by their different classifications. Moreover, in the instant case, the search for antibodies and the methods of detecting the protein complex or polypeptides are not coextensive. Groups III and VII encompass molecules which are claimed in terms of gene mutation, measuring the activity of the protein, measuring the binding between the drug and protein, drugs capable of modulating the activity of protein complex, which are not required for the search of Group II. Moreover, the search for Groups III and VII would require a text search for the methods.

9. The antibody of Group II, the expression vector of Group VI are all unrelated because a polynucleotide of Group VI does not encode an antibody of Group II, and the antibody of Group II cannot be encoded by a polynucleotide of Group VI. Therefore the antibody of Group II and polynucleotide of Group VI are unrelated.

10. Groups II, IV, V, VIII, XIV, XV are unrelated products because their structures and modes of action are different. Group II is drawn to an antibody, Group IV is transgenic animal, and Group V is a cell or a cell line, Group VIII is a drug which can modulate the activity of the protein complex. The drug can be a peptide, an antibody, a small molecule, a nucleic acid, an antisense nucleic acid, etc., Group XIV is a device, comprising nucleic acids which do not encode the antibody of Group II, Group XVI is a device comprising many other structurally distinct antibodies, therefore they are directed to products that are distinct both physically and functionally, are not required one for the other. Moreover, each is capable of separate manufacture and use, and each requires separate searches.

11. Group II and Groups IX-XIII, XVI are unrelated because the product of Group II is not used or otherwise involved in the process of Groups IX-XIII and XVI.

12. Groups III, VII, IX-XIII, XVI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The instant specification does not disclose that these methods would be used together. The method of for diagnosing a physiological disorder in an animal (Group III), a method of screening for drug candidates and selecting modulators (Group VII, IX-XII), a method for treating a physiological disorder or modulating neuronal death (Group XIII), a method of making an isolated polypeptides (Group XVI) are all unrelated as they comprise distinct steps and utilize different products which demonstrates that each method has a different mode of operation. Each invention performs this function using

a structurally and functionally divergent material. Moreover, the methodology and materials necessary for diagnosing a physiological disorder, screening for drug candidates and selecting modulators, making isolated polypeptides differ significantly for each of the materials. For diagnosing a physiological disorder (Group III), a protein complex is detected in a tissue extract, the ability of proteins to form a protein complex is assayed, and gene mutation is detected, for screening a drug and selecting a modulator (Groups VII, IX-XII), a large number of compounds from a pre-selected library are tested, the binding between the compound and protein complex is measured, and the inhibition of the activity of protein complex by said compound is determined, for treating a physiological disorder or modulating neuronal death (Group XIII), a compound capable of modulating the protein complex is administered to a patient; for making a protein complex (Group XVI), an expression vector and host cell is required. For these reasons the Inventions III, VII, IX-XIII, XVI are patentably distinct.

The inventions of Groups VII, IX-XII further differ from each other in that the assay used to screen for a drug is different. For inventions of Group VII, the amount of protein complex formed in the presence and absence of said drug is measured; for inventions of Groups IX, the activity of the protein of the protein complex in the presence or absence of said drug is measured; for inventions of Groups X, the binding between the drug and protein complex is measured; for inventions of Group XI, an interaction between the first protein and second protein is measured; for inventions of Group XII, providing atomic coordinates defining a 3D structure of a protein complex is required; For these reasons, the inventions of Groups VII, IX-XII are patentably distinct.

Furthermore, the distinct steps and products require separate and distinct searches. Because these inventions are distinct for the reasons given above and the searches for these groups are not coextensive, it would be burdensome to search the inventions of Groups III, VII, IX-XIII and XVI together.

13. Group IV, V, VI, XIV, XV and Groups III, VII, IX-XIII, XVI are unrelated because the products of Group IV, V, VI, XIV and XV are is not used or otherwise involved in the process of Groups III, VII, IX-XIII, and XVI.

14 Group VIII and XIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the drug can be used to diagnose a disease or used as a ligand to bind a receptor as opposed to be used for in vivo treatment of a physiological disorder.

Searching the inventions of Group VIII and Group XIII together would impose serious search burden. The inventions of Groups VIII and XIII have a separate status in the art as shown by their different classifications. Moreover, in the instant case, the search for drugs and the methods of treating a physiological disorder using said drug are not coextensive. Group XIII would require a text search for the method of treating a physiological disorder or modulating neuronal death.

15. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

16. This application contains claims directed to the following patentably distinct species of the claimed invention:

Applicant is required to elect a single species from the group consisting of penetratins, *l*-Tat_{49-57}, *d*-Tat_{49-57} ,retro--inverso isomers of *l*- or *d*-Tat_{49-57}, L-arginine oligomers, D- arginine oligomers, L-lysine oligomers, D-lysine oligomers, L-histine oligomers, D-histine oligomers, L-ornithine oligomers, D-ornithine oligomers, short peptide sequences derived from fibroblast growth factor, Galparan, and HSV-I structural protein VP22, and peptoid analogs thereof.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, 92, 102, 107 and 116 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include

all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

17. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

18. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

19. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance

with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hong Sang
Art Unit: 1643
Aug. 24, 2005

CHRISTOPHER YAEN
PATENT EXAMINER